**OBJECTIVE**

- To understand differences in mechanism of action (MoA) and pharmacodynamics (PD) between alemtuzumab and cladribine in the treatment of MS

**INTRODUCTION**

- MS therapy targeting T and B lymphocytes have different mechanisms of action and vary in efficacy and safety.
- Alemtuzumab’s humoral and CD52 mononuclear toxicity is approved in Europe.
- Cladribineprodrug is phosphorylated (initially by deoxycytidine kinase) to active 2-CdATP.

- Alemtuzumab selectively binds to CD52 to deplete circulating T and B lymphocytes, mainly within 1 month of treatment initiation.
- Cladribine interferes with DNA synthesis and repair to cause T- and B-cell apoptosis, resulting in partial depletion of T and B lymphocytes within 6–12 months of treatment.

- Durable efficacy was demonstrated up to 7 years with 53% of patients not receiving additional alemtuzumab (prior to their 2nd course) or other immunomodulatory therapy.

- Alemtuzumab and cladribine are both approved as non-continuous treatment, a need exists to differentiate their benefits and understand potential effects and safety implications in order to ultimately inform clinical decision-making.

**METHODS**

- A comprehensive review of published literature, congress abstracts, and pharmacodynamic profiles were performed to gather information on the MoA and PD of alemtuzumab and cladribine.

**RESULTS**

- Alemtuzumab and cladribine target T and B cells, but have distinct mechanisms that are not fully elucidated.

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**CONCLUSIONS**

- Alemtuzumab selectively binds to CD52 to rapidly deplete circulating T and B lymphocytes within 1 month of treatment initiation.

- A distinct pattern of lymphocyte repopulation then occurs following each treatment course, with CD4+ / CD8+ T- and CD19+ B-lymphocyte levels repopulating within 6–12 months of treatment; there are also alterations in some lymphocyte subsets as well as a shift from pro- to anti-inflammatory cytokine profiles.

- Cladribine interferes with DNA synthesis and repair to cause T- and B-cell apoptosis, resulting in partial depletion of T and B lymphocytes within 6–12 months of treatment.

- CD4+ T- and CD19+ B-cell counts recover over an extended timeframe following the second treatment course; cladribine may also modulate the cytokine profile.

- These distinctions in MoA and PD may underlie differences in short- and long-term efficacy and safety of alemtuzumab and cladribine.